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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/614,115

07/03/2003

Vladimir Baranov

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EXAMINER

COOK, LISA V

ART UNIT

PAPER NUMBER

1641

DATE MAILED: 10/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/614,115	Applicant(s) BARANOV ET AL.	
	Examiner Lisa V. Cook	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) 30-36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-29 is/are rejected.
- 7) ☒ Claim(s) 15-18 is/are objected to.
- 8) ☒ Claim(s) 1-36 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>see attached</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I (claims 1-29) in the response filed 7/27/06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 30-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Presently, claims 1-29 are under consideration.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on PTO-1449 has cited the references they have not been considered. For example see pages references listed through out the disclosure and on pages 78-84.

3. The information disclosure statements filed 11/4/03, 11/8/04, 7/25/05 and 5/16/06 have been considered as to the merits before First Action.

Drawings

4. The drawings are objected to under 37 CFR 1.84(h)(5) because Figure 9 show(s) modified forms of construction in the same view. Specifically the drawing is not clearly labeled. The labels are overlapping and appear to be numbers imposed with letters. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

5. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

I. The use of the trademarks has been noted in this application. (i.e. SEPHAROSE and TWEEN - see pages 46 and 50 for example). They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Objections

6. Claims 15-18 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

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Specifically, claims 15-18 are directed to the source of the atoms or atomic ions and/or the measurement of the element. However, these limitations are directed to methods using the kit and do not further limit the kit itself. Accordingly, these claims do not provide positive limitation to the kit found in independent claim 1. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 15, 17, and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 15 is vague and indefinite in reciting the “source of atoms or atomic ions” and subsequently reading on atomic detection systems. It is suggested that the claims clearly recite that the kit comprises one of the parameters selected from the specific components listed in the claim. Appropriate correction is required.

B. Claim 17 and 18 are vague and indefinite in reciting the *use of* an instrument because the instant claims read on a product not a method. The claims should be written to specific recite the inclusion of the instruments within a kit embodiment in order to be given patentable weight. Please clarify.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negative by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 1-5, 10-14 and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879).

Cais discloses a method of tagging biologically active material (column 7 lines 9-42) with metals (label/transition elements). The metals include manganese (atomic number 25), silver (atomic number 47), gold (atomic number 79), Cobalt (atomic number 27), iron (atomic number 26), and nickel (atomic number 28). See Table 1. Accordingly the patent to Cais reads on Applicants claims regarding a transition element having an atomic number of 21-29, 39-47, 57-79 or 89.

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The metal (label) is conjugated to the biologically active material by an unnatural bound or covalent (chemical) bound. See column 8 line 36 through column 9 line 21 and column 10 lines 56-66.

The tagged biological active material (labeling substance and binding component) are mixed with a sample (ligand) to form a tagged complex. The bound complexes are separated from unbound material. Either the bound or unbound aliquot is measured for the metal content. Column 3 lines 5-22. The metal can be measured via a variety of detection systems including emission spectrophotometer. See column 6 lines 29-42.

Cais also teaches the detection of any transition element/metal in specific binding assays and kits. See column 11 lines 45-66.

Although Cais teaches the reagents required by the claims; it does not specifically teach the reagents in kit configurations including buffers and instructions. However, kits are well known embodiments for assay reagents. Foster et al. (U.S. Patent #4,444,879) describe one example. In their patent kits including the reactant reagents, a microplate, positive controls, negative controls, standards, various buffers, and instructions are taught. The reagents are compartmentalized or packaged separately for utility. See figure 6, and column 15, lines 10-34.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the detection assay reagents and kits as taught by Cais and format them into a kits including buffers and instructions because Foster et al. taught that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit.

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Further, the reagents in a kit are available in pre-measured amounts, which eliminates the variability that can occur when performing the assay. Kits are also economically beneficial in reagent distribution.

It is also worth noting that the printed matter on instructions merely teaches the use of an existing product, and thus cannot impart patentability. See *In re Ngai*, 5/13/04, Michel, Gajarsa, Linn, per curiam. In other words the printed matter on the instructions in a kit cannot serve to define the kit over the prior art. See *In re Gulack*, 217 USPQ (CAFC 1983).

II. Claims 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879) and further in view of Maggio (Immunoenzyme technique I, CRC press © 1980, pages 186-187).

Cais in view of Foster et al. differ from the instant invention in not specifically teaching reagent immobilization (bound to solid support).

However, Maggio disclose enzyme immunoassays wherein either the antigen or antibody is immobilized onto a solid phase. The solid phase can be particles, cellulose, polyacrylamide, agarose, discs, tubes, beads, or micro plates (micro titer plates). See page 186. The reagents can be bound to the solid support by covalent linkage or passive adsorption (non-covalent means). See page 187 1st paragraph. Maggio taught that solid supports such as test strips "are very convenient to wash thereby reducing labor in assay procedures". Page 186, last line.

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It would have been obvious to one of ordinary skill in the art at the time the invention was made to immobilize assay reagents on solid support surfaces as taught by Maggio in the assay method/kit of Cais in view of Foster et al. because Maggio taught that reagent immobilized solid supports "are very convenient to wash thereby reducing labor in assay procedures". Page 186, last line. Absent evidence to the contrary the immobilization of reagents is deemed and obvious modification of the assay kits taught by Cais in view of Foster et al.

III. Claims 15-18 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879) and further in view of Neilsen et al. (Spectrochimica Acta Part B, 53, 1998, 339-345).

Please see Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879) as set forth above.

Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879) differs from the instant invention in not teaching reagents for the analyses related to laser ablation inductively coupled plasma-mass spectrometry and gel electrophoresis.

However, a procedure and reagents useful in inductively coupled plasma-mass spectrometry and further comprising electrophoresis is taught by Neilsen et al. Neilsen et al. employed both immunoelectrophoresis and laser ablation inductively coupled plasma (ICP)-mass spectrometry for the identification and quantification of metal binding proteins in blood serum.

Human serum was enriched with commercially available Co (Cobalt-supplied by Merck) was subjected to electrophoresis and the agarose gels corresponding to the 1st and 2nd dimensions were interrogated and analyzed using a Nd Yag laser (1064 nm) interfaced to ICP-mass spectrometry. See abstract, page 341 – 2.2. Neilsen et al. taught that electrophoresis is a powerful separation procedure (page 340, 1st column, 2nd paragraph) and laser ablation is a versatile solid sampling tool in ICP-spectrometry (page 340, 1st column, 3rd paragraph). The combination provided a novel route for studying metal protein distribution in serum (peak response was linear with concentration and the method showed precise replication (6% RSD), with a detection limit of 0.29ng. See abstract and page 345 Conclusion.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure transition elements (tags) linked to antibodies in the laser ablation inductively coupled plasma-mass spectrometry in combination with gel electrophoresis as taught by Neilsen et al. in the method/reagent kits of Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879), because Neilsen et al. taught that the electrophoresis is a powerful separation procedure (page 340, 1st column, 2nd paragraph) and laser ablation is a versatile solid sampling tool in ICP-spectrometry (page 340, 1st column, 3rd paragraph). The combination provided a novel route for studying metal protein distribution in serum (peak response was linear with concentration and the method showed precise replication (6% RSD), with a detection limit of 0.29ng. See abstract and page 345 Conclusion.

One having ordinary skill in the art would have been motivated to do this to acquire the enhanced sensitivity, wherein accurate and precise detection is rapidly available.

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IV. Claims 19 and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879) and further in view of Anbar (U.S. Patent #4,002,876).

Please see Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879) as set forth above.

Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879) differ from the instant invention in not specifically teaching that the element is an isotope or ion.

However, Anbar discloses a methods and reagents for tagging antibodies or antigens (biologically active material) with stable isotopes of certain elements or long-lived radioisotopes of these elements (transition elements). A known amount of the tagged antigens or antibodies are mixed with an unknown (analyte) to form an antigen-antibody complex. The bound complexes are separated from unbound material. Either the bound or unbound aliquot is via negative mass spectrometry to count the tagged atoms. See abstract and column 3 lines 25-41. The option of employing different labeling atoms to allow for the simultaneous measurement of a number of antigens is disclosed in column 6 lines 10-21. A system for detecting and measuring according to the disclosed method is seen in figures 1, 2, and 3. The method and reagents taught by Anbar gave higher sensitivity and allowed for the extension of immunoassays beyond their present limitations. See column 6 lines 22-28.

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It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure isotope or ion transition elements as taught by Anbar in the method/reagent kits of Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879) because Anbar taught that this gave higher sensitivity and allowed for the extension of immunoassays beyond their present limitations. See column 6 lines 22-28.

V. Claims 22 and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879) and further in view of Crooke (WO 99/451450).

Please see Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879) as set forth above.

Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879) differs from the instant invention in not specifically teaching methods/reagent kits utilizing a plurality of tagged transition elements linked to a plurality of biologically active.

These limitations are taught in the methods/reagents of Crooke et al. Crooke et al. are drawn to mass spectrometric methods for biomolecular screening. See abstract. The method provides for screening ligand or combinatorial libraries of compounds against one or more than one biological target molecules. See abstract. In other words the methods provide for the determining the interaction between one and a plurality of molecular species. See page 1, especially lines 17-19. In one embodiment different molecular weight tags (distinguishable element tags) are utilized to detect different nucleic acid targets (biologically active materials). See page 10, line 19 for example.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure a plurality of biologically active materials bound to transition elements (tags) as taught by Crooke et al. in the method/reagent kits of Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879), because Crooke et al. taught that his method significantly accelerated screening efforts because multiple targets could be screened simultaneously against large numbers of compounds. See page 10 line 25-27. This would reduce processing time, allowing for more data on various compounds simultaneously.

VI. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879) and further in view of Mire-Sluis et al. (Journal of Immunological Methods, 186, 1995, pages 157-160).

Please see Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879) as set forth above.

Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879) differs from the instant invention in not specifically teaching methods/reagent kits wherein the analyte is a cytokine.

However, Mire-Sluis et al. teach immunoassays to measure cytokines. See abstract. They further disclose that cytokines regulate the maintenance and function of the haematopoietic and immune systems. Their involvement in a wide variety of clinical disorders has led to the development of numerous assays to measure their presence *in vitro* and *in vivo*. Cytokine levels are also important as potential useful indicators of the presence and severity of a number of disorders. See page 157 1st column.

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It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure a cytokine as taught by Mire-Sluis et al. in the method/reagent kits of Cais (US Patent #4,205,952) in view of Foster et al. (US Patent #4,444,879), because Mire-Sluis et al. taught that cytokines regulate the maintenance and function of the haematopoietic and immune systems. Their involvement in a wide variety of clinical disorders has led to the development of numerous assays to measure their presence *in vitro* and *in vivo*. Cytokine levels are also important as potential useful indicators of the presence and severity of a number of disorders. See page 157 1st column.

One of ordinary skill would have been motivated to detect cytokines in order to assess disorders.

9. For reasons aforementioned, no claims are allowed.

Remarks

10. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Crooke et al. (US Patent #6,428,956) disclose methods of determining structure, site, and nature of the interaction between ligands and biomolecular targets via mass spectrometric analysis.

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11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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10/6/06



LONG V. LE

10/12/06

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